Brief Summary of the Circulatory System Devices Panel Meeting – September 12, 2013

Summary

A meeting of the Circulatory System Devices Panel was held on September 12, 2013, to have discussions on, and have the Panel make recommendations regarding the 515(i) order for the membrane-lung for long-term pulmonary support (21CFR 868.5610). The membrane-lung for long-term pulmonary support are one of the remaining pre-amendment Class III medical devices currently cleared for marketing through the 510(k) pathway. A membrane-lung for long-term pulmonary support, as defined in the current regulation, is a device used to provide to a patient extracorporeal blood oxygenation for longer than 24 hours.

21 CFR 868.5610, membrane lung for long-term pulmonary support refers to the oxygenator component of an extracorporeal circuit for long-term procedures, commonly referred to as ECMO. However, many components make up the extracorporeal circuit for ECMO use. Currently, there are no regulations defining the other extracorporeal circuit components that comprise an ECMO circuit (long-term durations of use). As such, a broader definition and identification is being proposed and a realignment of the classification regulation to include 1) all of the circuit components/accessories needed for long-term extracorporeal support, and 2) flexibility for current technology, to provide an efficient approach to regulate an entire system that provides and/or participates in long-term extracorporeal support.

The Panel discussion involved making recommendations regarding regulatory classification to either reconfirm to class III or reclassify to class I or class II. To this end, the Panel was asked to provide input on the risks to health, safety, and effectiveness of extracorporeal circuit and accessories for long-term pulmonary/cardiopulmonary support. The panel was also requested to weigh in on the FDA's proposed premarket regulatory classification strategy for extracorporeal circuit and accessories for long-term pulmonary/cardiopulmonary support which included reclassification from Class III to Class II for conditions where an acute (reversible) condition prevents the patient's own body from providing the physiologic gas exchange needed to sustain life in conditions where imminent death is threatened by respiratory failure (e.g., meconium aspiration, congenital diaphragmatic hernia, pulmonary hypertension) in neonates and infants, or cardiorespiratory failure (resulting in the inability to separate from cardiopulmonary bypass following cardiac surgery) in pediatric patients.

FDA Proposed Regulation and Classification for ECMO devices

21 CFR 870.4100 *Extracorporeal circuit and accessories for long-term pulmonary/cardiopulmonary support*:

(a) *Identification*. An extracorporeal circuit and accessories for long-term pulmonary/cardiopulmonary support (>6 hours) is a system of devices that provides assisted extracorporeal circulation and physiologic gas exchange of the patient's blood where an acute (reversible) condition prevents the patient's own body from providing the physiologic gas exchange needed to sustain life in conditions where imminent death is threatened by respiratory failure (e.g., meconium aspiration, congenital diaphragmatic hernia, pulmonary hypertension) in neonates and infants, or cardiorespiratory failure (resulting in the inability to separate from cardiopulmonary bypass following cardiac surgery) in all pediatric patients. An acute reversible or treatable cause of respiratory or cardiorespiratory failure should be evident, and the subject should demonstrate unresponsiveness to maximum medical and/or ventilation therapy. The main components of the system include, but are not limited to, the console (hardware), software and disposables, including but not limited to, an oxygenator, blood pump, heat exchanger, cannulae, tubing, filters, and other accessories (e.g., monitors, detectors, sensors, connectors).

(b) Class II (special controls).

Panel Deliberations

The Panel heard FDA, Industry, and Public presentations regarding the regulatory history, clinical use, and the data available for extracorporeal circuit and accessories for long-term pulmonary/cardiopulmonary support. After all presentations, the Panel had several questions for FDA as well as the public speakers. Following the question/answer period, the Panel deliberated amongst themselves, where the following (major) issues were raised:

- Regulation of specific components under a regulation defined for a circuit
- How new devices would fit into this construct
- ECMO (pulmonary and cardiopulmonary support) vs. VAD (cardiac support) indications for pediatric and adult populations
- Specific indications for use for devices currently cleared for ECMO
- Adult ECMO – whether adult indications should also be considered since adult ECMO use has increased recently (e.g., cardiac arrest, pulmonary emboli, refractory cardiogenic shock, BTT, H1N1, Cystic Fibrosis)
- Whether bridge-to-decision or bridge-to-transplant indications should also be considered in the pediatric population
- How FDA will ensure that significant modifications made to the devices will come in for review under the 510(k) paradigm
- How we can improve the collection of MDR data to be more meaningful to FDA post-market surveillance

- Use of registries for adverse event data

The discussion regarding the lack of adult data presented to the panel dominated the panel discussions. FDA attempted to outline the construct of the 515(i) program, and that the reclassification discussions are intended for the devices that have been cleared. In summary, the indications for use that have been cleared since 1976 were very broad, however, the design of the device(s) (e.g., sizes) and the clinical data provided (e.g., for the oxygenator) to support long-term use were for the infant/neonatal/pediatric patient populations (*one exception was the Avalon Catheter which was reviewed in the wrong branch and did include adult size cannulae – although the predicate was for infants only*). The Panel indicated that use in adults has increased significantly in recent years, and so they would like FDA to review all of the available adult literature and reconsider broadening the proposed indications intended for reclassification to adult populations (if appropriate).

FDA Questions

At the end of the meeting, the Panel addressed 4 FDA questions related to the original proposal (with the understanding that FDA will re-review the available adult literature and broaden the proposal if indicated). In conclusion, the Panel (as well as the industry, patient, and consumer representatives) unanimously agreed with FDA's proposal as identified above, regarding the reclassification of membrane-lung for long-term pulmonary support from Class III to Class II Special Controls as specifically indicated for the neonatal, infant, and pediatric patient population.

Below is a summary of the Panel's responses to the FDA questions, as well as a summary of an informal vote of the Panel members regarding the reclassification of membrane-lung for long-term pulmonary support:

Q1 - risks to health for extracorporeal circuit and accessories for long-term pulmonary/cardiopulmonary support

The panel believed that the list of risks to health outlined by the FDA should also include information on the following:

Renal dysfunction
Neurologic injury
DIC-coagulation covered in more broad language
Transfusion issues
Inflammatory response

FDA Response: Most of the items identified by the panel are adverse events, and not risks to health. A discussion ensued regarding risks to health vs. adverse events, and the panel generally agreed that the risks to health were complete. ***The Panel would like FDA to consider expanding the definition of Adverse Tissue Reaction to ensure that it truly captures inflammatory response***.

Q2 – safety and effectiveness for extracorporeal circuit and accessories

The panel discussed the available scientific evidence and agreed that it is adequate to support the safety and effectiveness for extracorporeal circuit and accessories for long-term pulmonary/cardiopulmonary support with the definitions provided, but there is discomfort surrounding the terms safe and effective (it is really more a decision of benefit/risk), and the long-term outcome of the patients (hard to determine whether long-term events are related to the ECMO therapy or the underlying condition).

Q3 – special controls for extracorporeal circuit and accessories for long-term pulmonary/cardiopulmonary support – Pediatric uses

The panel generally felt that the list of special controls was adequate but compatibility of circuit components needs to be evaluated. Additionally, the issue of duration of use should be considered, e.g., is there a time at which the device is no longer safe or effective?

Q4 – Classification

The panel believed that extracorporeal circuit and accessories for long-term pulmonary/cardiopulmonary support are life-supporting. The panel agreed with the reclassification proposal to Class II for the pediatric population but would like to see more information regarding the adult population in order to give a recommendation on that population – and to use this reclassification process most efficiently to reclassify all appropriate intended uses.

PANEL Informal Vote on Proposed Classification

Class II for extracorporeal circuit and accessories for long-term pulmonary/cardiopulmonary support as proposed	**13**

(The industry, patient, and consumer reps agreed with Class II as well)

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